How Good Is the Evidence Linking Breastfeeding and Intelligence?

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ABSTRACT. ***Background.*** **We conducted a critical review of the many studies that have tried to determine whether breastfeeding has a beneficial effect on intellect.**

Design/Methods. **By searching Medline and the references of selected articles, we identified publications that evaluated the association between breastfeeding and cognitive outcomes. We then appraised and described each study according to 8 principles of clinical epidemiology: 1) study design, 2) target population: whether full-term infants were studied, 3) sample size, 4) collection of feeding data: whether studies met 4 standards of quality—suitable definition and duration of breastfeeding, and appropriate timing and source of feeding data, 5) control of susceptibility bias: whether studies controlled for socioeconomic status and stimulation of the child, 6) blinding: whether observers of the outcome were blind to feeding status, 7) outcome: whether a standardized individual test of general intelligence at an age older than 2 years was used, and 8) format of results: whether studies reported an effect size or some other strategy to interpret the clinical impact of results.**

Results. **We identified 40 pertinent publications from 1929 to February 2001. Twenty-seven (68%) concluded that breastfeeding promotes intelligence. Many studies, however, had methodological flaws. Only 2 papers studied full-term infants and met all 4 standards of high-quality feeding data, controlled for 2 critical confounders, reported blinding, used an appropriate test, and allowed the reader to interpret the clinical significance of the findings with an effect size. Of these 2, 1 study concluded that the effect of breastfeeding on intellect was significant, and the other did not.**

Conclusion. **Although the majority of studies concluded that breastfeeding promotes intelligence, the evidence from higher quality studies is less persuasive.** ***Pediatrics*** **2002;109:1044–1053;** ***breastfeeding, infant feeding, intelligence, cognition, meta-analysis.***

ABBREVIATIONS. WISC-R, Wechsler Intelligence Scale for Children-Revised; HOME, Home Observation for Measurement of the Environment.

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Many studies in the medical and psychological literature have examined the relationship between breastfeeding and cognitive outcomes.[1–40] Some of these studies report a direct positive effect, ie, that breastfeeding an infant results in that child growing up to be smarter than non-breastfed peers. Other studies show very little significant difference between the intellect of children who were and were not breastfed as infants. Currently, it is difficult to know how to interpret studies with contradictory findings or how to assess new studies that are published and describe this association.

The central methodological predicament in performing such a study is that it is neither feasible nor ethical to assign breastfeeding randomly to mothers. Therefore, the environment and the mothers of breastfed children are inherently different from those of infants whose mothers either choose not to breastfeed or experience difficulty breastfeeding.[9,41] The task of the investigator, therefore, is to disentangle the subtle effect of breastfeeding an infant from the consequences of the larger environment. Determining the result of breastfeeding alone using an observational study design is challenging. Techniques of clinical epidemiology exist, however, to help minimize the possibility of biased findings. In this study, we propose a set of methodological standards with which to assess observational studies linking breastfeeding and intelligence. Using these criteria, we give a "best evidence" review of published studies linking breastfeeding and intelligence.

METHODS

Identification of Articles

To identify studies investigating the association between breastfeeding and intelligence or other cognitive outcomes, we searched the literature using Medline from 1966 to February 2001 and cross-referenced the subject heading "breastfeeding" and "intelligence" or "cognition." Articles published only in a non-English language were excluded. Titles and available abstracts were reviewed to find appropriate studies from this initial list, and the bibliographies of relevant articles were then searched for additional studies. A study was included if it independently assessed the relationship between breastfeeding and a cognitive outcome. "Breastfeeding" included breastfeeding itself, breast milk, or choice to breastfeed. "Cognitive outcomes" included: general IQ; speech or language tests; the achievement of developmental milestones; mathematics; logic; reasoning ability; educational achievement; copying designs or visual-motor integration; developmental delay; or learning disorders. Tests of motor ability alone were not included.

If a study cited a previous study that described the methods in greater detail, information from the previous article was included in our evaluation. Unpublished materials or reports, however, were not included in our evaluation.

The classification scheme and the methodological standards were chosen by consensus of the 3 authors a priori to the evaluation of articles. Similar to previous critical reviews,[42] these criteria were based on principles of clinical epidemiology as they apply to observational studies.[43] Each study was reviewed individually by each of the 3 authors and then again as a group. If there was disagreement regarding the evaluation of any particular article, the article was reviewed again until consensus was reached.

Evaluation of Articles

For each study, we examined the overall design of the study and 7 important methodological aspects (sample size, target population, quality of feeding data, control of susceptibility bias, blinding, outcome measures, and format of results). In addition, we describe the authors' conclusions—whether, in the summary or abstract, the authors state that breastfeeding has a positive or no effect on cognition.

1. Study Design

We classified studies using 3 categories of research design: birth cohorts, school registry cohorts, and case-control studies.

Studies were classified as birth cohorts if patients were selected at birth or at the time of infant feeding and followed forward in time to the point when the outcome was assessed. For example, the cohort of infants could be population-based, sampled by exposure to type of feeding, or represent a convenience sample. Birth cohort studies provide an opportunity for an accurate depiction of subjects' baseline state. Although feeding is not assigned experimentally, investigators can evaluate the similarity between feeding groups, assess problems that are introduced if patients withdraw from the study, and ensure equal detection of outcomes. In addition, these cohort studies give greater opportunity for accurate assessment of confounders. Because of these advantages of birth cohort studies over other observational studies, we considered them to be "core" studies of higher quality.

Studies were classified as school registry cohorts if children were selected by a listing of students at a school or school district. Feeding history was then obtained retrospectively; outcomes were obtained close to the time of the sampling. An advantage of these studies is the relative ease with which they are accomplished. In addition, blinding of observers and uniform detection of outcomes can be accomplished. School registry cohorts may be at risk of finding biased associations, however, because investigators have limited knowledge of the circumstances that led to the particular distribution of students in the school (eg, children with severe cognitive impairment or high ability may not be in "mainstream" classrooms). Although feeding history may theoretically be obtained accurately from historical records, details about the baseline state, feeding method, and confounders are often irretrievable.

Case-control studies were classified separately. In a case-control study, children are sampled by the outcome status (usually in 2 groups—cases with cognitive impairment and controls without impairment), and feeding history is then obtained. Case-control studies are vulnerable to many of the same limitations as school registry cohorts, but can yield valid results if, among other concerns, suitable controls are selected.

2. Sample Size

Studies should be adequately powered to find a clinically meaningful difference between feeding groups. Because different investigators may disagree about the size of a clinically significant effect of breastfeeding, we estimated what might constitute an appropriate sample size based on the following assumptions: 1) If a 5-point difference in IQ (0.33 standard deviation) between feeding groups on a standardized test such as the Wechsler Intelligence Scale for Children-Revised (WISC-R) is considered meaningful, a study with 80% power (2-sided α error = 0.05) would require at least 142 children in each group. 2) If a 3-point difference in IQ (0.20 standard deviation) between feeding groups is considered meaningful, a study with 80% power (2-sided α error = 0.05) would require at least 393 children in each group, 3) For a 1-point difference, 2500 children in each group would be required, and 4) If one were looking for a 10-point difference, only 36 children in each feeding group would be required. Power calculations are especially relevant when studies find no effect because a true difference between study groups can be mistaken for no difference when the sample size is too small. Because power calculations are often not reported in studies and there is no agreed-on definition of a clinically significant effect size, we did not hold studies to a set standard of sample size. Instead, we listed the sample size for each study in the results, and readers can, therefore, make their own assessments regarding appropriate sample size.

3. Target Population

When evaluating studies, it is important to know the target population to assess the generalizability of results. Accordingly, we have separated studies that evaluated outcomes in preterm infants exclusively from other investigations. Because preterm infants have increased nutritional requirements and distinct developmental outcomes compared with term infants, it is unclear the extent to which results in preterm infants are applicable to term infants, and vice versa.

4. Quality of Feeding Data

For each study, we determined the presence or absence of 4 components of data on breastfeeding. An ideal study would meet all of the following criteria:

- Definition of "breastfeeding:" Investigators should indicate whether infants received breast milk exclusively or with supplemental formula or other foods.
- Timing of data collection: Feeding data should be obtained during infancy (when the feeding was occurring) rather than after the first year of life when details of feeding history are more vulnerable to errors of recall. In addition, feeding data should not be obtained solely within the first few weeks after birth when women are likely to change feeding method.[44]
- Source of feeding data: Feeding data should be obtained from the mother or from health records, rather than from another relative or a lactation consultant.
- Duration of breastfeeding: Because feeding methods often change in the first few weeks after birth,[44] we considered whether authors specified that infants were breastfed for at least 1 month (4 weeks), irrespective of the exclusivity of breastfeeding.

5. Control of Susceptibility Bias

A major controversy with studies that attempt to determine whether breastfeeding improves cognition is whether susceptibility bias (confounding) is minimized. Bias can be introduced if a factor, associated with both exposure (the decision to breastfeed a child) and outcome (intelligence), is not part of the causal pathway of that association. We examined 2 factors that are particularly relevant to the research question and have been documented to be related independently to both type of feeding and outcomes on intelligence tests: socioeconomic status/parental education, and quality and quantity of stimulation of the child (including social interactions).

Socioeconomic Status of the Family

Most experts agree that socioeconomic status is a factor in the choice of feeding method[41,45] and also affects a child's intelligence.[46,47] Little agreement exists, however, about the appropriate measure of socioeconomic status. Thus, we considered any control or adjustment for parental occupation, income, educational level, or any combination of these variables to be an adequate assessment of the influence of socioeconomic status. Many other variables, such as maternal or paternal intelligence, marital status, number of children, and maternal age are, to some degree, markers of socioeconomic status. These variables, however, are not clearly related to both feeding method and intelligence independent of socioeconomic status, and were not considered to be among the "crucial" confounders.

Stimulation of the Child

The quality and quantity of stimulation a child receives, both from parental interactions and other social interactions, influence the results of cognitive or intelligence tests in that child.[46,48,49] Because breastfeeding is currently considered a nurturing or positive behavior in many industrialized societies, mothers who choose to breastfeed or are successful at breastfeeding may be more inclined to nurture or stimulate their children in a variety of other ways.[9,50] To control adequately for the stimulation a child receives, a study should measure the quality or quantity of stimulation or interactions a child receives at nonfeeding times. Examples of suitable variables include the Child Experience Checklist[51] or the Home Observation for Measurement of the Environment (HOME).[52]

Each study was reviewed to determine whether these 2 factors were measured and used in the analysis of the results (eg, matching or statistical adjustment). We considered the measurement of a variable at a single point in time to be adequate, although recognizing that socioeconomic status and the stimulation a child receives may vary over time.

Other variables used in studies as part of adjustments for baseline differences are noted and listed in the appendix under nine major categories: family characteristics, parental characteristics, pregnancy factors, perinatal factors, child characteristics, child behaviors, factors related to intelligence testing, feeding factors, and other factors.

6. Blinding

Outcomes should have been measured by observers who were blind to feeding status. In some situations, blinding of the observer to feeding method may be compromised. For example, if parents are asked to report on their child's achievement in school, recall of whether the child was breastfed (or for how long) may be affected; such an outcome would not be considered blind to feeding status.

7. Outcome Measures

To be considered "appropriate," we required that the outcome be a standardized individual measure of general intelligence and that the assessment be done when the child was at least 2 years of age. Although researchers have used many approaches to assess cognitive outcomes, we considered measures of only 1 aspect of cognitive function, such as receptive language, to be too limited; and measures of achievement were too closely linked to educational experience rather than "innate" intelligence. Screening tests such as the Denver II Developmental Screening Test[53] were also considered inappropriate, because the test is intended to screen for clinical abnormalities, not to discern relatively small, individual differences of intellect in normal children.[54]

If a study measured >1 outcome, we looked for the use of a standardized individual test of general intelligence at age 2 years or greater, and did not evaluate other supplementary outcome measures. If multiple appropriate outcomes were reported, we recorded the outcome measured at the oldest age.

8. Format of Results

Studies should provide an assessment of the clinical significance of the results after adjustment for potential confounders. In other words, authors were expected to provide a meaningful interpretation of the size of the difference between the groups being compared, such that physicians could explain the feeding effect to interested parents. Acceptable methods included reporting effect size, comparison with norms in the population at-large, and standard deviations. If the authors did not report effect size within the study itself, but we were able to calculate an effect size from standard deviations or norms from *Tests in Print*[55] or developmental textbooks,[54,56,57] the study was considered to have met this standard.

9. Authors' Conclusions

In addition to evaluating the studies using the 8 criteria, we reviewed the abstracts and summaries of the papers to discern an overall tone to the conclusions, specifically to determine whether the authors concluded that breastfeeding improves intelligence or whether they were skeptical about the relationship.

RESULTS

We identified 40 publications[1–40] from 1929 to February 2001 that examined the link between breastfeeding and cognitive outcomes. Tables 1 and 2 describe the results of the methodological evaluation of the studies.

Study Design

Of the 40 eligible studies, 30 (75%) were birth cohorts (27 with full-term children), 2 randomized, controlled trials in preterm children, 5 (14%) school registry cohorts, and 3 case-control studies (Table 1).

Target Population

Thirty-five (88%) articles either studied populations of mixed full-term and preterm infants,[2,9–11,14,24,25,27–32,37–39] only full-term infants,[1,7,16,19,22,23,26,33–35,40] or did not specify[3–6,12,13,15,20] the gestational age or birth weight of the study samples. These studies were collectively classified as full-term studies. Most of the studies that had both full-term and preterm infants were population-based, and thus the vast majority of infants were full-term. The remaining 5 (12%) articles[8,17,18,21,36] studied the association of breastfeeding with cognition in low birth weight (and presumably preterm) infants exclusively.

Sample Size

The total sample size used in the studies is reported in Table 1. When sample sizes varied depending on the outcome assessed, we listed the number of children included for the appropriate test of general intelligence at the highest age. The sample sizes varied from 50 to >11 000.

Quality of the Feeding Data

The quality of feeding data varied considerably in the studies (Table 1). Only 9 (23%)[1,14,16,29,30,34,38,40,58] of 40 met all 4 criteria regarding the quality of feeding data; 8 were full-term birth cohorts. For example, a study with high-quality feeding data[29] specified the breastfed groups as those that "mostly breastfed;" feeding status was determined at multiple times (at birth, 6 weeks, and 3, 6, 12, and 18 months); information was obtained by interviewing the mother at each of those times; and the duration of breastfeeding was more than a month in the "breastfed" group.

Of the 31 studies that did not meet this standard, 15 (48%)[2–5,9,10,12,18–22,31,33,39] did not adequately define breastfeeding by failing to report whether infants only received breast milk or were supplemented with formula or food. In the 2 reports from the randomized, controlled trial,[17,36] the "breastfeeding group" of preterm infants received donor breast milk, which was probably mature milk and may not represent the nutritional adequacy or other benefits found in milk from an infant's own mother that is matched to the gestational age of the child. In addition, the banked milk may have been primarily composed of drip milk, which is notably low in fat and unsuitable for use as full diet. In those studies, the control group received preterm formula. Thus, although these studies may have technically met the standard for appropriate definition of breastfeeding, they answer a different question than the other investigations. In the 2 preterm observational birth cohorts, which did not meet the standard for appropriate definition of breastfeeding,[18,21] the authors defined breastfeeding as the "intent to breastfeed," and did not confirm actual breastfeeding. Although 1 of these studies[18] did perform a separate analysis of "successful breastfeeders," no definition of "successful" was given.

TABLE 1. Studies Linking Breastfeeding and Intelligence: Sample Size, Quality of Feeding Data, and Control for 2 Critical Factors That Reduce Susceptibility Bias

Study Design and First Author	Publication Year	Sample Size	Definition of Breastfeeding	Timing of Data Collection	Source of Feeding Data	Duration of Breastfeeding	Socioeconomic Status	Stimulation of the Child
				Full-Term Studies				
Observational birth cohorts								
Rogerson[30]*	1939	111	+	+	+	+	+	−
Dörner[7]	1978	134	+	+	−	+	−	−
Rodgers[28]†	1978	1398	+	−	+	+	+	+
Silva[31]†	1978	1037	−	−	+	+	+	+
Fergusson[9]†	1982	954	−	−	+	+	+	+
Ounsted[24]	1984	242	+	−	−	−	+	−
Taylor[32]	1984	11 024	+	−	+	+	+	−
Morrow-Tlucak[22]†	1988	275	−	+	−	+	+	+
Pollock[25]	1989	8146	+	−	+	−	+	−
Bauer[3]	1991	50	−	−	−	−	+	−
Jacobson[15]†	1992	323	+	+	−	+	+	+
Rogan[29]*	1993	636	+	+	+	+	+	−
Pollock[26]	1994	3838	+	−	+	+	+	−
Temboury[33]	1994	229	−	−	−	+	+	−
Agostoni[62]*	1995	86	+	+	+	+	+	−
Florey[10]	1995	592	−	−	+	−	+	−
Gale[11]	1996	994	+	+	+	−	+	−
Johnson[16]*†	1996	204	+	+	+	+	+	+
Niemala[23]	1996	726	+	−	+	+	+	−
Wang[34]*	1996	145	+	+	+	+	−	−
Agostoni[1]*	1997	90	+	+	+	+	+	−
Barros[2]	1997	1363	−	+	+	+	+	−
Horwood[14]*	1998	799	+	+	+	+	+	−
Malloy[37]	1998	518	+	−	+	+	+	−
Richards[27]	1998	511	+	−	+	−	+	−
Wigg[38]*†	1998	375	+	+	+	+	+	+
Lucas[19]	1999	447	−	+	+	+	+	−
School registry cohorts								
Hoefer[13]	1929	383	+	−	+	+	−	−
Broad[4]	1972	134	−	+	+	+	−	−
Broad[5]	1975	185	−	+	+	+	−	−
Greene[12]	1995	432	−	−	+	+	+	−
Innis[40]*	1996	400	+	+	+	+	−	−
Case-control studies								
Menkes[20]	1977	82	−	−	+	+	−	−
Burd[6]	1988	100	+	−	+	−	−	−
Tanoue[39]	1989	369	−	−	+	−	−	−
				Preterm Studies				
Randomized birth cohorts								
Lucas[17]†	1989	502	+	+	+	−	+	+
Lucas[36]†	1994	502	+	+	+	−	+	+
Observational birth cohorts								
Morley[21]	1988	746	−	−	+	−	+	−
Doyle[8]	1992	201	+	−	−	−	+	−
Lucas[18]	1992	300	−	−	+	−	+	−

+ Met criterion.
− Did not meet criterion.
* Meets all 4 criteria for high quality feeding data.
† Controlled for both socioeconomic status and stimulation of the child.

TABLE 2. Blinding, Outcome Measures, Format of Results, and Authors' Conclusions

Study Design and First Author	Publication Year	Blinding‡	Appropriate§ Test	Primary Outcome Variable	Age at Assessment	Format of Results	Reported Effect Size After Adjustment‖	Authors' Conclusions
				Full-Term Studies				
Observational birth cohorts								
Rogerson[30]*	1939	+	−	School achievement	5–10 y	+	7% vs 39% below average in school	Advantage
Dörner[7]	1978	−	−	School reports	16 y	+	0.7 points on a 5-point scale	Advantage
Rodgers[28]†	1978	−	+	Nonverbal tests	15 y	+	0.176 SD	Advantage
Silva[31]†	1978	−	−	Peabody Picture Vocabulary Test	3 y	−	NS	Null
Fergusson[9]†	1982	+	+	WISC-R	7 y	+	0.334 SD	Null
Ounsted[24]	1984	−	−	Human figure drawing test	5 y	+	1.095 or of higher scores if breastfed	Advantage
Taylor[32]	1984	−	−	English Picture Vocabulary Test	5 y	+	0.17 SD	Advantage
Morrow-Tlucak[22]†	1988	+	+	Bayley Mental Development Index	2 y	+	0.667 SD	Advantage
Pollock[25]	1989	−	+	British Ability Scales-reasoning	7–1/2 y	+	1.1 SD	Null
Bauer[3]	1991	−	+	McCarthy Scales¶	3 y	−	"Remained Significant"	Advantage
Jacobson[15]†	1992	−	+	McCarthy Scales¶	4.1 y	−	Regression coefficient = 0.06 (NS)	Null
Rogan[29]*	1993	−	+	McCarthy Scales¶	5 y	+	0.32 SD	Advantage
Pollock[26]	1994	−	+	British Ability Scales	10 y	+	0.205 SD	Advantage
Temboury[33]	1994	+	+	Bayley Mental Development Index	18–29 mo	+	1.92 OR; lower scores if bottlefed	Advantage
Agostoni[62]*	1995	−	+	Brunet-Lézine's scale	4 mo	+	0.523 SD	Advantage
Florey[10]	1995	+	−	Bayley Mental Development Index	18 mo	+	0.313 SD	Advantage
Gale[11]	1996	+	−	AH4 IQ	60–70 y	+	0.009 SD (NS)	Null
Johnson[16]*†	1996	+	+	Stanford-Binet Intelligence Scale	3 y	+	0.288 SD	Advantage
Niemala[23]	1996	−	+	Columbia Mental Maturity Scale	4.67 y	−	"Correlated with scores"	Advantage
Wang[34]*	1996	−	−	Denver Developmental Screening	1 y	+	79% of vs 64% passed	Advantage
Agostoni[1]*	1997	−	+	Brunet-Lézine's scale	24 mo	+	0.09 SD (NS)	Null
Barros[2]	1997	−	−	Denver Developmental Screening	12 mo	+	25% vs 42% abnormal	Advantage
Horwood[14]	1998	−	+	WISC-R	8–9 y	+	0.164 SD	Advantage
Malloy[37]	1998	+	+	WISC-R	9–10 y	+	0.1 SD (NS)	Null
Richards[27]	1998	−	−	Pidgeon-Revised	8 y	−	0.01 point for those ever breastfed (NS)	Null
Wigg[38]*†	1998	+	+	WISC	11–13 y	+	0.053 SD (NS)	Null
Lucas[19]	1999	−	−	Bayley Mental Development Index	18 mo	+	0.09 SD (NS)	Null
School registry cohorts								
Hoefer[13]	1929	−	+	Stanford-Binet Intelligence Scale	7–13 y	+	0.375 SD	Advantage
Broad[4]	1972	+	−	11 speech tests	5–6 y	−	*P* values	Advantage
Broad[5]	1975	+	−	11 speech tests	5–6 y	−	*P* values	Advantage
Greene[12]	1995	−	+	Raven's Standard#	11–16 y	+	5.4–6.0 percentile points	Advantage
Innis[40]*	1996	+	−	Fagan Test of Infant Intelligence	39 wk	+	0.5% looking at novel stimulus (NS)	Null

TABLE 2. Continued

Study Design and First Author	Publication Year	Blinding‡	Appropriate§ Test	Primary Outcome Variable	Age at Assessment	Format of Results	Reported Effect Size After Adjustment‖	Authors' Conclusions
Case-control studies								
Menkes[20]	1977	+	−	Learning disorder	7 y	+	14% of LD breastfed, 47% of controls	Advantage
Burd[6]	1988	−	+	PDD		+	13% of PDD breastfed, 11% of controls (NS)	Null
Tanoue[39]	1989	−	+	Infantile Autism (IA)	3 y	+	25% of IA weaned <1 wk, 7% of controls	Advantage
Preterm Studies								
Randomized birth cohorts								
Lucas[17]†	1989	+	−	Knobloch's Screening Inventory	9 mo	+	(neg) 0.21 SD	Null
Lucas[36]†	1994	+	−	Bayley Mental Development Index	18 mo	+	0.1 SD (NS)	Advantage
Observational birth cohorts								
Morley[21]	1988	−	−	Bayley Mental Development Index	18 mo	+	0.269 SD	Advantage
Doyle[8]	1992	−	+	WISC-R	8 y	+	0.213 SD (NS)	Null
Lucas[18]	1992	−	+	Abbreviated WISC-R	7.5-8 y	+	0.553 SD	Advantage

OR indicates odds ratio; NS, not significant; PDD, pervasive developmental disorder.
+ Met criteria.
− Did not meet criteria.
* Meets all 4 criteria for high-quality feeding data.
† Controlled for both socioeconomic status and stimulation of the child.
‡ Observers of outcome blind to exposure.
§ Standardized individual test of general intelligence at age 2 years or greater.
‖ Effect is positive for breastfeeding unless otherwise indicated (neg) and when range was given, mean effect size is shown.
¶ McCarthy Scales of Children's Abilities.
\# Raven's Standard Progressive Matrices Test.

Of the 31 studies, in 21 (67%),[3,6,8–10,12,13,18,20,21,23–28,31–33,37,39] the reports did not meet the standard for timing of data collection because the feeding information was obtained either too late or too early. In some,[6,8,9,13,20,26–28,31,32,37,39] the authors obtained feeding history from parents when the child was 2 years or older, and recall of details of the feeding may therefore be inaccurate or incomplete. Many studies[10,18,21,25,26,28] collected feeding data at the time of birth or shortly thereafter, when feeding status was likely to change; and others[3,12,23–25,33] did not indicate when the data were collected.

Most studies did describe an appropriate source of feeding data, using either an interview with the mother or health records. One study,[10] however, used both health records and maternal interviews, and found inconsistent recordings in the health record.[10] This type of inconsistency may lead to inaccurate classification in the other studies[4,5,11,12,20,23,30] that relied on historical records, but the use of archived data did not address whether feeding information was always available for every child.

Twenty-seven (68%) of the 40 studies [1,2,4,5,7,9,12–16,19,20,22,23,26,28–35,37,38,40] included a feeding group for whom breastfeeding duration was at least 1 month.

Susceptibility Bias

Nine studies (23%)[9,15–17,22,28,31,36,38] controlled adequately for both socioeconomic status and level of stimulation (Table 1). For example, 1 investigation[9] measured socioeconomic status as family socioeconomic status and maternal education, and quantified stimulation using a Child Experience Checklist,[51] a 30-item checklist designed to measure the range of the child's experiences up to age 4 years and shown to be highly correlated with intelligence and language development. In addition, this study controlled for maternal training in child rearing,[59] maternal intelligence, gestational age and birth weight of the child, and gender of the child. We considered the 2 critical factors to be controlled adequately by randomization in the reports from the randomized, controlled trial.[17,36]

Thirty[1–3,8–11,14–19,21–33,35–38] of the full-term and preterm birth cohorts and 1 of the school registry cohorts[12] controlled for socioeconomic status. As shown in the appendix, considerable variation was found in number and type of "noncritical" confounders included in the analyses of these studies. Two studies[4,5] gathered information on potential confounders but did not use the information in the adjusted results, and another study[26] tested 76 potential confounders in bivariate analysis and then retained only those 8 that were statistically significant.

Blinding

Only 15 (38%)[4,5,9–11,16,17,20,22,30,33,36–38,40] of 40 stated that observers of the outcome were blind to feeding status (Table 2). Other studies may have used observers who were unaware of feeding status but did not report this information. One study used a computer examination to test cognition, and we considered this to be adequate blinding.

Outcome Measures

Twenty-two (55%)[1,3,6,8,9,12–16,18,22–24,26,28,29,33,35,37–39] of the 40 studies used an appropriate measure of cognition, ie, a standardized individual test of general intelligence measured at 2 years of age or older (Table 2). Of the 18 remaining studies, some did not meet the standard for >1 reason. For example, 8[10,15,17,19,21,34,36,40] measured outcomes in children <2 years of age, and 3 studies[25,31,32] assessed general intelligence using picture vocabulary tests, considered a poor assessment of general intelligence.[49] Two studies[7,30] used only school achievement to measure cognition, and 1[11] used a group test in adults aged 60 to 70 years (in relation to breastfeeding during infancy). The latter study also used group tests, administered with a computer,[11] which are not considered to be as reliable as individually administered tests. In addition, it seems implausible that differences in intellect at age 60 to 70 years can be attributed to feeding from infancy, without consideration of many life experience factors. Three studies[2,17,34] used screening measures to assess cognition. One study[25] assessed intelligence at 5 years of age using the Human Figure Drawing Test.[25] Although some "drawing persons" tests have been validated as tests of general intelligence, figure drawing also has been used to screen for emotional disturbances and depression. The Human Figure Drawing Test itself is a subtest of 2 more general tests to assess academic readiness and to screen for problems in preschool.[55] In 2 related studies,[4,5] 11 nonstandardized speech tests were used as the outcomes of interest, without more general tests.

One case-control study[20] used the presence of a learning disorder, which was not operationally defined, as its outcome measure. The other 2 case-control studies[6,39] used the diagnoses of pervasive developmental disorder and infantile autism, respectively, as outcome measures. These diagnoses were made using standardized criteria and were thus considered appropriate tests. Although pervasive developmental disorder and autism are related to intellect but are not tests of general intelligence, we included these studies because they examined the notion that breastfeeding promotes neurodevelopment and, therefore, cognition.

Format of Results

As shown in Table 2, 33 studies (83%)[1,2,6–14,17–22,24–26,28–30,32–34,36–40,58] reported some way to interpret the clinical significance of results, and 21 (53%)[1,8–11,13,14,17–19,21,22,26,28,29,32,34–38] allowed calculation of an effect size. Most studies reported differences in actual scores on standardized tests for which we were able to find normative values and standard deviations. Two studies[23,31] that did not meet the standard for effect size showed a discrepancy in scores between breastfed and formula fed children, but did not describe the difference in scores after adjustment. Another report[3] stated that breastfeeding was "significantly correlated with scores" and showed results only as correlation coefficients and *P* values; we did not consider this study to have met the standard for reporting. Two studies[25,33] reported results in odds ratios (odds of having a higher or lower developmental score by feeding group), but did not report enough data about the rates of the outcome to calculate a true effect size. Because one can explain to parents the concept of "the odds of having an above average child," however, we considered odds ratios an acceptable expression of clinical significance.

Authors' Conclusions

Among 40 studies, 13 (32%)[1,8,9,11,15,17,19,25,27,31,37,38,40] did not claim a causative link (Table 2). Seven[9,11,15,27,31,37,38] of these found that the effects of breastfeeding, statistically significant in the unadjusted analysis, became insignificant when controlling for socioeconomic status, stimulation, or other factors. The 2 reports from the randomized trial showed that preterm formula was equivalent to[36] or better than[17] donor breast milk for the cognitive development of preterm infants.

Papers That Duplicated the Patient Sample

Although 40 separate papers were published, 2 pairs of studies,[1,9,31,35] a trio of studies,[25,26,32] and 4 preterm studies[17,18,21,36] investigated the same sample or subsets of the same sample, resulting in studies of only 33 different groups of children. In the reports from the randomized, controlled trial,[17,36] preterm formula was compared with banked (probably full-term) breast milk. Although the same children are involved, 2 related reports[18,21] compared outcomes in the children whose mothers intended to breastfeed versus children of mothers who did not intend to breastfeed, irrespective of randomization.

Quality of Studies

Only 2 studies[16,38] met all the methodological standards. In the most recent,[38] researchers followed 375 children in South Australia from birth in 1979 to 1982 until the age of 11 to 13 years. Feeding data were recorded at 6 months old. Structured interviews were conducted periodically to obtain demographic, medical, and environmental information. The Daniel Scale[38] was used as a measure of parental socioeconomic status and was measured 2 times (6 months of age and again at 11–13 years). The quality of the child's environment was judged by the HOME inventory-24 at ages 3 and 5. At 11 to 13 years old, the children were assessed using the Wechsler Intelligence Scale for Children by examiners who were unaware of the child's feeding history. The 3.8 point (mean = 100, standard deviation = 15) advantage seen in breastfed children was reduced to a nonsignificant 0.8 point difference after adjustment. These authors concluded, therefore, that "any beneficial effect of breastfeeding on cognitive development is quite small in magnitude."

In the other best study,[16] investigators followed 211 white children of normal birth weight longitudinally from birth to age 3. Breastfeeding information was obtained at birth and biweekly thereafter for 2 years. When the children were 2 years old, the family's socioeconomic status and HOME score were assessed. At age 3 (± 4 weeks), the intelligence of the children was measured using the Stanford-Binet Composite IQ Scale by examiners who were blind to the feeding history. Children who were breastfed had mean IQ scores that were 5 points (standard deviation = 16) higher than those never breastfed; this difference was slightly reduced to 4.6 points after controlling for socioeconomic status, HOME scores, mother's intelligence, maternal smoking, gender, and birth order.

Among the 7 other studies[9,15,17,22,28,31,36] (not including the 2[16,38] just described) that controlled for both socioeconomic status and stimulation/interaction of the child, 3[22,28,36] concluded that breastfeeding promotes cognitive development, and 4[9,15,17,31] did not.

DISCUSSION

An ideal observational study to measure the true effect of breastfeeding on intelligence would follow full-term infants longitudinally, define and measure breastfeeding with sufficient detail and appropriate timing, control for socioeconomic status and the stimulation a child receives, measure intelligence using a standardized instrument at age 2 or greater by observers unaware of feeding status, and report an effect size or some other metric to interpret the quantitative magnitude of results. We evaluated published studies linking breastfeeding and intelligence according to these methodological standards. Although the majority of studies concluded that breastfeeding promotes intelligence, the evidence from higher quality studies is less convincing. The 2 "best" studies disagreed. Of the 7 other studies that controlled for both socioeconomic status and stimulation a child receives, 3 concluded that breastfeeding promotes intelligence, and 4 did not.

Previous investigators[42] have evaluated the quality of studies examining the relationship between breastfeeding and infections and found that high-quality studies showed only a minimally protective effect of breastfeeding on rates of infection. Their report also proposed standards for how to perform future investigations on the same topic. Similarly, we generated standards for studying the impact of breastfeeding on intelligence and applied them to the studies found in the literature.

A recent study[60] evaluated 24 studies linking breastfeeding and intelligence according to methodologic criteria established for that investigation. These investigators concluded that the question has not been "comprehensively answered" but that 4 of 6 studies that met their 3 standards found a 2- to 5-point advantage in cognitive development for term infants. The 3 standards were clearly defined outcome, specification of partial versus exclusive breastfeeding, and control of confounding.

Our study differs in several ways from this previous "best-evidence" review.[60] We consider control of confounding or the minimization of susceptibility bias to be the critical issue when examining this literature. Therefore, we required studies to control for 2 factors proven to be related to both feeding method and intelligence. In contrast, the authors in the other study required studies to control for 1) maternal/familial factors and 2) infant characteristics, without specifying what those factors or characteristics need be. For example, many studies controlled for birth order. The relationship between birth order and breastfeeding is not clearly established. Although birth order may still act as a confounder in some studies, it is not one that is likely to modify substantially the effect of breastfeeding. In addition, we attempted to include all published studies whereas these authors focused on studies of infants born since 1960 because formulas before that time were substantially different from current formulas.

Also in contrast to our findings, a recent meta-analysis[61] on the effect of breastfeeding on intelligence concluded that breastfeeding does confer an intellectual advantage. The meta-analysis did not, however, attempt to evaluate each study's methods or interpret results on the basis of the quality of the investigation. As a result, the pooled effect estimates obtained reflect the average of a heterogeneous group of studies. Our systematic review, unlike a meta-analysis, attempts to provide a better understanding of the strengths and limitations of each study's methodology and its relationship to the study's results.

Although the current review followed methods similar to previous investigators[42] who examined the effects of breastfeeding on infection, limitations of our methodology exist.[62] For example, our selection of methodological standards may not be acceptable to all investigators. These standards were chosen, however, by consensus a priori to the evaluation of particular studies, and are consistent with basic principles of clinical epidemiology.[43] Another limitation is that we evaluated information available in published articles only and did not attempt to reach authors for additional details about study methods nor did we seek unpublished studies. In this context, we assumed that the important studies would be published. In addition, although we assumed that key information about the methodology would be published, we do recognize that the space limitations of journals may result in the omission of important details regarding the quality of a study. Studies whose main purpose was other than the determination of the feeding-intellect relationship may be particularly disadvantaged in our assessment.

Although the majority of studies concluded that breastfeeding promotes intelligence, the evidence from higher quality studies is less persuasive. We conclude that no convincing evidence exists regarding the comparative effects of breastfeeding and artificial feeding on intelligence. Future investigators are urged to use more rigorous methods and criteria in the design of studies on breastfeeding.

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APPENDIX 1. Other "Noncritical" Factors That Introduce Susceptibility Bias

Category of Factor Included in Adjustment	Reference Number of Study
Family characteristics	
Race/skin color	12,21,25,28,37,57
Birth order/parity	8,10,11,13,15,20,26,35,38,57,63
Number of siblings/family size	22,25–28,31,32
Inter-pregnancy interval	57
Single parent/marital status	13,19–22,38,57
Psychosocial risk	32
Parent factors	
Maternal intelligence	9,14,15,21,27,34,38
Parental interest in education	26,27
Maternal age	8,10,11,13,19–21,27,28,31,32,35,38,57,63
Mother working	13,32
Maternal training in child rearing	9
Maternal malaise	31
Pregnancy factors	
Alcohol	8,21,28
Smoking	8,13,15,21,22,25,28,31,38,57
Child's characteristics	
Gestational age	1,8,9,11,13,31,57,63
Birth weight	1,8–11,13,16,20,21,28,37–39,57
Weight of child at age 1	10
Gender	2,3,4,6,8–11,13,15,18–20,22,26,28,31,32,37,38,63
Lead level	38
Height/age	1,57
IQ*	6
Child behaviors	
Shyness	32
Tantrums	32
Hyperactivity	32
Dummy (pacifier) use	10,57
Behavior score	31
Testing factors	
Age of child at testing	6,18,21,28,31,37
Identification of the examiner	28
Feeding factors	
Prenatal class attendance	25
Pesticide exposures	21
Perinatal factors	
Place of birth	16,19,25,32
Type of delivery	20,22,63
Days of ventilation	20,63
Illness of the child	18,39,57
Other feeds	63
Age at weaning	26
Other factors	
Main caretaker	57
Use of day care center	27,57

* Controlled (matched) for IQ when assessing outcome of Pervasive Developmental Disorder.

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